PARASITE CONTROL: A GLOBAL CHALLENGE

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Introduction

The population growth, the rapidly increasing urbanization and the growth in income in developing countries are creating a tremendous increase in the demand for food of animal origin. This revolution, the "livestock revolution" is demand driven illustrated by the fact that the meat consumption in developing countries grew approximately three times more than it did in the developed world during the period from early 1970s to the mid 1990s. During the same period the production of animal food products also grew most dramatically in the countries with the increased demand. In fact the meat production in developing countries with the exception of Sub-Saharan Africa grew more than five times the rate in the developed countries. (1)

The projections of the International Food Policy Research Institute (IFPRI) using the IMPACT (International Model for Policy Analysis of Agricultural Consumption) are that the consumption of meat and milk in developing countries will grow by about 3% per year between now and 2020. (2)

It is likely that this will improve the livelihood of small and medium scale market oriented farmers but only if an enabling environment is created including access to credit, development of infrastructure and animal production and health services. Farmers need access to information regarding disease control and livestock management supporting their ability to make decision where to invest their resources to increase production and productivity.

Parasitic Diseases. A Global Problem

Globally parasitic diseases together with other diseases continue to be a major constraint on profitable livestock production. They are rarely associated with high mortality and easily identifiable clinical signs and their effects are usually characterized by lower outputs of animal products, by-products, manure and traction all contributing to production and productivity losses. However parasitic diseases are repeatedly recognized by livestock owners, particularly small ruminant producers as one of the constraints preventing animals from reaching their full production potential and it is generally accepted that the cost of control of most of these is the responsibility of the animal owner.

Although the parasitic diseases are distributed throughout the world they have different impact according to production system, management and geo-climatic conditions. In industrialised production systems the greatest impact is not on the loss of productivity but more likely related to the cost of control with considerable resources spent on parasiticides. There is, however, a possible shift in this as the importance of anthelmintic resistance keep growing with decreased efficiency and a likely increase in the production losses in these production systems (3). For example there is a real risk that the dependency of the Australian woolgrowers on drenching to control worms will become obsolete within 10 years due to anthelmintic resistance. Consequently the cost of gastro-intestinal nematodes to the Australian wool industry currently estimated at AUS$220 million could skyrocket to AUS$700 million within the same time frame. (4)

In mixed farming systems and extensive grazing systems in the tropics and subtropics the environment is usually very suitable for parasite development and the variety and prevalence of parasitic diseases are much greater than in temperate climates adding substantially to the disease problems. The result is often reduced productivity expressed in the form of reduced weight gain, delayed and weak oestrus and lower calving rates but perhaps an even greater impact is the lost potential.

The importance of ticks and tick borne diseases, tsetse flies and trypanosomosis have been recognized for many years and the structure and functions of many veterinary services in the tropics and sub-tropics reflect the fact that the public good assumed responsibility for the control of these diseases. There is however also a growing awareness of the importance of less dramatic parasitic infections (helminths, flies, mites, lice) as part of the multitude of production related diseases which are a constraint for the much needed productivity increase of livestock in developing countries.

A recent OIE commissioned, FAO implemented survey of OIE member countries tried to assess the perception of the national veterinary services concerning the importance and ranking of parasitic diseases dividing them into five groups; helminths, ticks, mange mites, flies and lice. Unfortunately, more than 65% of the countries surveyed have not carried out any detailed studies, and the result is based on estimates. In order to establish a balanced and accurate profile of the member countries' perception the ranking of the parasite groups were weighted according to the number of 1^{st}, 2^{nd}, 3^{rd} and 4^{th} rankings received and allocated points accordingly. This led to helminths being assigned 38.9% of the total points for all categories; ticks, 23.7%; mange mites 15.4%; Diptera of veterinary importance, 15.2%; and lice, 6.8% reflecting the opinion of the OIE member countries replying to the questionnaire.

Many of the countries (85.7%) consider that they have a significant market for antiparasitic agents. As chemical compounds with very few exceptions have been the sole means used by agricultural and livestock producers for controlling parasitic diseases comparing the market for antiparasitic agents with that for other consumables (antibiotics, vaccines, sera) is a good indicator of the relative importance attributed to parasite control by the livestock owners/countries. (5) In 1998, world sales of endoparasiticides, endectocides and ectoparasiticides (COMISA figures) were in the region of 3,700 million dollars (6). The demand for parasiticides differs from one geo-economic area to the other depending on production systems and the composition of parasite populations.

Economic Impact

The host-parasite interactions and the effect of the parasites on their hosts are complex reactions and influence directly or indirectly the production and productivity of the animal. The major effects are related to feed intake, which is reduced, and to the protein metabolism. The protein losses caused by the parasites stimulate the compensatory liver synthesis of nutrients, which require energy and protein. This will be obtained from resources normally canalised into production of wool, meat and milk with subsequent losses in production. (7)

The losses can be categorized into those affecting the productivity of individual animals and those influencing herd productivity. Among the first are mortality, lower market value (slaughter house condemnations), reduction in body weight gain, reduced wool and milk yield, reduced draught power, changed dung output (fuel, fertilizer) and reduced efficiency in feed conversion. The second category includes the reduced productive life of the animals, the disturbance of the genetic selection effort and the possibility to maintain and improve the herd. (7)

In addition there may be an effect of the infection on human welfare such as the reduced supply of protein and other effects on community development related to reduced traction and dung output. The picture wouldn't be complete without a calculation of the effect of control on the productivity of animals.

Thus there is general agreement that the parasitic diseases are important and cause considerable losses but the extent of the losses needs to be accurately calculated. It has however proven difficult to evaluate the economics of diseases and animal health interventions due to the complex relationships between animal health and impact on production, access to markets and the non-production benefits of livestock. In addition the knowledge base regarding economics of treatment is inadequate. (8)

The estimated or potential losses caused by endo- and ecto-parasites have been compiled from published material. The methods used to assess the losses are often subjective but they do provide an estimate of the impact caused by these parasites.

In Nigeria one study estimated that 11% of the value of sheep and goat production was lost per year (9) and another estimated the annual losses caused by GI nematodes in Northern Nigeria to be approximately US$40 million (10). In Kenya losses due to Haemonchus infection has been estimated to US$26 million annually (11). The losses experienced in industrialized production system can also be substantial and during the late 1980s the US Department of Agriculture estimated losses due to biting flies to be approximately US$1,500 million per year, mites US$259 million, ticks US$104 million, lice US$38 million and other insects US$296 (12). The annual losses in ruminants caused by GI nematodes were estimated at US$300-400 million and the expenses incurred to control the worms are in the range of US$140 million Ref.. Similarly the livestock industry in Australia has also incurred substantial losses. The annual cost of major parasites in Australia was calculated in 1994 using a costing model separating the production losses from the control cost. According to this the losses caused by ticks in cattle was AUS$132 million and the losses for sheep including worms, lice and blowflies were AUS$552. (13)

Some impact assessments have also been made in Brazil, Argentina and Uruguay. It is known that, if not treated, the mortality in sheep flocks in Rio Grande do Sul is approximately 40%. Those surviving will produce 300-500 grams less wool and 2 - 5 kg less meat per animal. In addition the mating age will be delayed for 6-12 months. For Rio Grande alone, with its more than 11,000,000 sheep, the losses would be substantial if no alternative treatment strategies will be available (14)(15). The impact in Argentina has been calculated for four geographical zones with different degrees of anthelmintic resistance. The total annual loss in this country is approximately US$20-21 million (16)(17). Studies in Uruguay have shown that the mortality in a non - parasite control scenario will be approximately 50% with a reduced body weight and fleece weight of 25% and 29% respectively after the first year. The estimated total losses of fleece weight alone is estimated at 18 million kegs which amounts to an economic loss of about US$42 million. (18)

Chemical Control

The host-parasite relationship will over time evolve into endemic stability and it is a well-known fact that many indigenous livestock breeds are resistant/resilient to parasites. With the intensification of production and the introduction of new breeds the need for control of parasites and pests increased. Throughout the last century the pharmaceutical industry has been able to continuously develop increasingly effective new compounds the application of which enabled the veterinarian/farmer to control a large number of different economically important parasites and their associated diseases.

The access to these efficient drugs and chemicals and the easiness by which they could be applied, combined with the improved diagnostic tests and the immense progress made in establishing the epidemiology of parasites of ruminants led to a period of relative success in the control of pests particularly in the industrialized livestock production systems. However, the false assumption that parasite control was easy and could be accomplished by using the chemicals and drugs without an epidemiological database was also being promoted preventing or delaying the epidemiological studies which is a pre-requisite for effective control. (19)

Further complicating the situation today and for future parasite control programmes is the fact that all the economically important parasite species of sheep and goats and some of cattle have developed resistance to all four groups of anthelmintics. In the last decade, almost one century after the first reports of arthropod resistance to pesticides for agricultural use (20), we have seen an almost exponential increase in new cases of resistance in various parasite species affecting agriculture and public health in many geo-climatic areas of the world. (21), (22), (23)

Resistance to Parasiticides

The definition of resistance used in this report is the «detection, by means of susceptibility tests, of a significant increase in individuals within a single species and population of parasites which are capable of tolerating doses of parasiticides that have proven to be lethal for most individuals of the same species».

Resistance is probably an inevitable consequence of the use of parasiticides and there is substantial evidence that when a parasite has developed resistance to one chemical/drug from a certain group it will usually also be resistant to other products from the same group. The speed by which a parasite develops resistance will depend on how severe the selection pressure is on the parasite population. It is known that this is linked to frequency of treatment and the fact that widespread and excessive use of these products, without considering the epidemiology/ecology of the parasites has led to the development of resistance of the parasites to the majority of existing drug categories. Under dosing, which is a common phenomenon favour the survival of heterozygous individuals, possibly enhancing the selection pressure for resistance. There is also evidence that strategic treatments, particularly at times when the free-living stages of gastro-intestinal nematode populations have been small have contributed to resistance development. Furthermore a substantial amount of cheap sub-quality drugs have been available on the market and this has undoubtedly contributed to the problem. (23), (24) However, what remains the key issue is that a moderate loss of efficacy (generally not perceived at field level) represents an enormous loss in terms of the antiparasitic agent's cost effectiveness, and a significant step along the path of no return in terms of resistance to parasiticides. For example, a reduction of 20% in the efficacy of an anthelmintic or acaricide at field level not only means a loss of efficacy equivalent to US$20 for every US$100 invested in veterinary products, but also represents a genetically based problem against the future sustainability of the whole chemical group. (5)

Resistance Diagnosis and Management

Diagnosis and control are two inseparable measures of any health programme, but in the case of resistance to antiparasitic agents, this relationship becomes even more crucial. In this case, it is not sufficient to merely know the species of parasites, it is also necessary to determine, as early as possible, the degree of susceptibility of the parasite populations to the available chemical groups (cross, or multiple resistance).

In the OIE survey referred to above (5), 54.5% of the replying countries indicated that they had diagnosed resistance in at least one group of parasites. There is almost certainly under-recording of the phenomenon, since the resistance of i.e. helminths, is not normally reported to Veterinary Services. It was also observed that 24.4% of the replying countries have to cope with the problem of resistance in more than three groups of parasites. This fact has only rarely been taken into account when the problem was considered at field level and control was planned. Thus it is increasingly frequent for the producer to experience «multi-resistance» which has developed simultaneously, not only to several groups of antiparasitic agents (25), but also in different species of parasites. Accordingly, any rational control programme should start by using this knowledge for developing diagnostic capabilities that make it possible to differentiate the effect of the antiparasitic agent on the target species for control from those non target species affected by the antiparasitic agent.

A lack of diagnosis does not mean that the problem does not exist; on the contrary, it often indicates a series of shortcomings, ranging from a failure to perceive the problem in the field, to the lack of capabilities to carry out laboratory diagnosis. Another difficulty, which has been of concern, is the lack of infrastructure required for the flow of disease information from the field to the laboratories and back. Furthermore the lack of proper techniques for diagnosing resistance is also among the main difficulties when it comes to maintaining a resistance-monitoring system. This situation underlines the fact that many governments lack information about the real impact of these problems and hinders the planning of proper control measures. (26),(27)

Potential Consequences

In view of the increasing problem with resistance to parasiticides, it will be difficult to continue to maintain a prevention and control approach that is based almost exclusively on the use of antiparasitic agents. This is a serious problem, which is further enhanced by the fact that we cannot expect a supply of new drugs in the nearest future. The pharmaceutical industry has seen continuously escalating research and development costs for the registration of new drugs. The cost of developing a new product is between 100 and 230 million dollars, for a process that can take more than 10 years from discovery of a potential candidate, to placing it on the market (28), (29). Antiparasitic compounds have to compete for funding with products for the benefit of other more profitable patients, specifically humans. (29) Thus, the antiparasitic agents for use in animal health must be viewed as a non-renewable resource and it is essential that we preserve and safeguard the drugs we have available and use them wisely.

This genetically based resistance in parasite populations has developed within the context of a world undergoing far-reaching political, social and economic changes, which must be taken into consideration when attempting to implement sustainable prevention and control measures. The scenario for the twenty-first century will be characterised by meat, wool and milk markets that are ever more globalised, competitive and demanding, especially with regard to freedom from residues and prevention of environmental contamination. Governments and industry will not have the same operational freedom as in the past and it is unlikely that there will even exist drugs to which parasites cannot develop resistance. Therefore even more attention needs to be directed towards preventing ecological imbalances (30), (31) and residues in meat, milk and wool. The failure to do this could turn into non-tariff barriers to trade between countries (32), (33), (34). Another situation preventing trade, both within and between countries, is the possibility of introducing resistant parasites through the transfer (35),(36) 43) or import of live animals. This is a widely recognised fact in the case of arthropods and is becoming more frequent in helminths (33), (37), (38), (39), (40).

Registration and Quality Control of Parasiticides

In many cases, it is difficult for Governments to maintain specialised staff and adequate facilities to support the registration and continuous quality control of parasiticides. Of the countries included in the above mentioned study 49.3 % reported that they were having difficulties in ensuring proper registration of antiparasitic agents (5). This basic government function is fulfilled only with great difficulty in developing countries, which are much more susceptible to problems of adulteration and the introduction of low-quality drugs. The principal difficulties mentioned by the Member Countries include: lack of proper legislation; lack of a specific registration unit; registration by other government units not specialised in animal health; total or partial lack of infrastructure to carry out the necessary analytical testing for each type of compound; the impossibility of ensuring continuing control over the quality of antiparasitic agents; and the failure to link registration with the occurrence of resistance in the field. During the present decade, generic antiparasitic agents have come to stay. It is not difficult these days to find countries where the same active ingredient is marketed under more than 20 different trade names. Competition between different formulations is healthy, provided of course that quality is maintained (which does not mean only the correct concentration of the active ingredient). This situation and the lack of training among users increase the consumption of cheap and often low-quality drugs. Without doubt this is the great challenge facing countries which do not yet have the capability to control the toxicity, residues and efficacy of antiparasitic agents.

Future Needs

It is important that all the parties involved - governments, the pharmaceutical industry, private and international organisations and most importantly veterinarians, extension personnel and livestock producers realize, that the time of easy parasite control based on the use of parasiticides only, is over. It is essential that perceptions and attitudes change with an understanding that parasite control in the future we will have to rely on a combination of strategies, which most likely will require more work and more monitoring (23), (24), (41).

The development and management of future sustainable integrated parasite control strategies require the capability within the areas of epidemiology, diagnosis of parasites and resistance of these, integrated pest management and the registration and quality control of parasiticides.

Epidemiology: The most important single requirement for the successful implementation of rational and sustainable parasite control programmes in grazing animals is a sound knowledge of the epidemiology of the parasites as they interact with their hosts in specific climatic, management and production environments (24). Epidemiology is the frame of reference on which the rational control of resistance must be based and although the importance of epidemiological knowledge in the prevention and control of resistance to antiparasitic agents is widely accepted, the epidemiological database of many developing countries is still incomplete. The availability of molecular techniques and appropriate mathematical models will provide tools for a better understanding of parasite population dynamics and help to minimise the selection for resistance (42).

Diagnosis: It is necessary to establish the capability, or strengthen the existing capability, for diagnosing resistance using duly standardised and harmonised techniques which make it possible to rationalise control measures without the indiscriminate use of antiparasitic agents.

Integrated pest management: Total dependence on a single method of control has proven to be non-sustainable and non cost-effective in the long term (23), (43), (44), (45). The terminology integrated pest management refer to the fact that all options for control (chemical, non-chemical) are considered for use following the determination of which parasites are economically important, their epidemiology, their resistance status and the production system/management structure being in place. Thus it is impossible to prepare standardized control strategies, which can be applied in all situations, and the approach would be to thoroughly analyse the situation and apply the ‘best bet’ options effectively combining several means of control as a way of creating sustainable strategies for managing parasite populations (46).

It is not anticipated that the use of chemicals can be completely replaced with other interventions. However, the selection pressure for resistance can be reduced by lowering the number of treatments, by only treating the animals which need treatment and by timing the treatments according to epidemiology making sure that a susceptible refugia of parasites remains in the environment. The potential problem of exposing the total population of parasites to the selection pressure can best be illustrated by the example of mites. When treating for mange mites, an obligate parasite with practically no refugia population, development of resistance will be enhanced by simultaneously exposing all parasitic stages to the treatments.

The principle of selective treatment has been practised in the past using levels of eggs per gram of faeces as cut off point for treatment. More recently the principle has been applied based on monitoring of the level of anaemia caused by *Haemonchus* using the FAMACHA[1] technique, a bioassay originally developed in South Africa (47). The process of field validation, training of personnel and distribution of the system is ongoing with FAO collaboration in South Africa, Paraguay and Uruguay.

The implementation of an IPM programme involves elements that are sometimes difficult to achieve in developing countries. These include the availability of results of applied research in epidemiological and control, a change of policy to further the application of methods that are less dependent on antiparasitic agents; and the participation of the producer and his veterinary advisor in training programmes. Some IPM systems are complicated to implement, but the routine use of computerised models makes it possible to rationalise control measures in a more global and economical manner (42), (48).

Registration and quality control of antiparasitic agents: It is during the registration process that the government authority approves the sale and use of an antiparasitic agent, after having evaluated whether the product is effective and that its use involves no risk for animals, public health or the environment. This process is often difficult for many developing countries because it requires sophisticated infrastructure and specialised personnel to carry out the tests. Notwithstanding this, some countries have made important advances both nationally and regionally. Another obligation which has proven more complicated to implement and for which the poorer countries are on their own is the continuous monitoring of the quality of antiparasitic agents in order to prevent abuses, including adulteration, the sale of substandard preparations and drug combinations of dubious stability.

The structural changes related to privatization, which has been introduced into the Veterinary Services in many countries, have resulted in a dramatic reduction in the capabilities of disease diagnosis and monitoring (26). This is jeopardizing the resistance management and it is, strongly advisable that developing countries and those in transition maintain or if lacking/dismantled establish a small critical mass of specialised professionals who can manage the four areas discussed above.

FAO Perspective

The parasite control programme of the Food and Agriculture Organization of the United Nations is continuously involved in the collection, analyses, collation and distribution of information related to the epidemiology, diagnosis and control of parasites and their associated diseases. This is done through regular contact with world leading scientists attending FAO or FAO/WHO Expert Consultations (49), the interaction with the FAO Collaborating Centres and the constant monitoring of the scientific literature.

Request for assistance from member countries related to their fight against ecto- and endoparasites and the subsequent technical input have often been aimed at improving diagnostic capability and establishing the epidemiological knowledge base creating the basis for the introduction of cost-effective and sustainable control systems. As examples of these programmes the integrated programme to control ticks and tick transmitted diseases in Africa and the eradication of *Amblyomma variegatum* in the Caribbean could be mentioned.

With the growing problem of resistance to antiparasitic agents, and the FAO's Animal Health Service, together with its Regional Offices, have made resistance management an important component of its programme. A permanent FAO working group "The Working Group on Parasiticide Resistance (WGPR) was established in 1997. This is a panel of experts, which advises the FAO on strategies for integrated parasite management (IPM) and resistance management. The WGPR gathers, organises and analyses information on the epidemiology, diagnosis and control of parasites and management of resistance to parasiticides, assisting the FAO in preparing guidelines for the diagnosis and control.

The FAO and the FAO/WGPR collaborate with the pharmaceutical industry through the FAO/Industry Contact Group on Parasiticide Resistance. The Industry is represented by the Veterinary Parasiticide Resistance Group (VPRG), a specialised COMISA[2] consultative group whose mandate is to advise industry and non-industrial organisations on the implications and consequences of resistance to parasiticides, and on monitoring and control strategies.

Considering the limited capability to diagnose resistance in parasites this issue particularly acaricide resistance in ticks has attracted the attention of governments, international institutions, the pharmaceutical industry and

[1] FAMACHA: Faffa Malan Chart
[2] COMISA: World Animal Health Industry Confederation

academic organisations (50), (51). This led to the establishment of the FAO's World Acaricide Resistance Reference Centre (WARRC) in Berlin, Germany (34). Unfortunately, this Centre has been defunct since 1996, due to funding problems, and the functions which was formerly carried out by WARRC are now being transferred to Regional FAO Reference Centres for Diagnosis and Monitoring of Acaricide resistance. Three Centres have been identified, located in Colombia (CORPOICA), Mexico (CENID-PAVET[3]), and Uruguay (DILAVE «Miguel C. Rubino»[4]) During the first phase, the Centres have the task of developing the region's technical capability for diagnosing and monitoring tick resistance to acaricides. The results of activities and information related to the work of the Centres will be disseminated through the FAO network on network on Ticks and Tick-Borne Diseases, coordinated by CORPOICA[5] in Bogota, Colombia. This Network also provide timely information on training courses, seminars and working meetings and the availability of duly harmonised and standardised diagnostic «kits».

In addition FAO has promoted and financially supported the creation of two electronic networks on helminths - one in Latin America (coordinated by INTA[6], Castelar, Argentina) and the other in Africa (coordinated by the Veterinary Faculty, Pretoria University, South Africa). In addition to the specific functions performed by these networks, the FAO will encourage interconnection and interaction between these and other existing networks.

In short, the collaboration between FAO, the WGPR, the INDUSTRY Contact Group, the FAO collaborating Centres and other international institutions and organizations aims at providing the required information and training for development of sustainable IPM and the appropriate management of resistance to parasiticides. In order to facilitate this a set of guidelines will be produced consisting of five modules, one for each of the five economically important groups of parasites, ticks, helminths, flies, mites and lice. Each module will be presented in a standardized format and it is the intention that each of the modules will serve as a guide to the diagnosis of resistance and act as a decision support system for selecting the 'best bet' options for integrated control and management of resistance to parasiticides

1 Annual Data. FAO Statistics Division, Food and Agriculture Organization (1999)

2 Delgado C, Rosegrant M, Steinfeld H, Ehui, S, Courbois C, Livestock to 2020: The next food revolution. International Food Policy Research Institute (IFPRI) *2020 Vision Brief* (1999) 61, 1-2

3 Perry B D & Randolph T F, Improving the assessment of the economic impact of parasitic diseases and of their control in production animals. *Veterinary Parasitology* (1999) 84, 145-168

4 LeJambre L, Personal communication (2000)

5 Nari A & Hansen J W, Resistance of Ecto- and Endo-parasites: Current and Future Solutions, 67th General Session. International Committee. OIE. Paris. 17-21 May. 1999. (1999)

6 COMISA, Personal communication, (1999)

7 Morris R S, How economically important is animal disease and why? In Dijkhuizen A A, Morris R S (Eds.) Animal Health Economics and Applications Post Graduate Foundation in Veterinary Science, University of Sydney, Sydney South (1997) 1-12

8 Tisdell C A, Harrison S R, Ramsay G C, The economic impacts of endemic diseases and disease control programmes, *Rev. sci. tech. Off. int. Epiz* (1999) 18 (2) 380-398

9 Schillhorn van Veen T W, Small ruminants health problems in Northern Nigeria with emphasis on Helminthiasis. *Nigerian Veterinary Journal* (1973) 2 26-31

[3] CENAPA: Centro Nacional de Investigaciones Disciplinarias en Microbiología
[4] DILAVE: Dirección de Laboratorios Veterinarios "Miguel C. Rubino"

[5] CORPOICA: Corporación Colombiana de Investigación Agropecuaria
[6] INTA: Instituto Nacional de Tecnología Agropecuaria

10 Akerejola O O, Njoku C O, Schillhorn van Veen T W, Ovine and caprine diseases in Nigeria: a review of economic losses, *Bulletin of Animal Health and Production in Africa* (1979) 27 (1) 65-70

11 Allonby E W, FAO sheep and goat project, Kenya, Annual Report (1975)

12 Kunz S E, Murrell K D, Lambert G, James L F, Terrill C E, Estimated losses of livestock to pests, In Hanson A A, Pimentel D, (Eds.) *CRC Handbook of pest Management in Agriculture*, 2nd edition (1989) Volume I 69-98

13 McLeod R S, Costs of major parasites to the Australian livestock industries, *Int. J. Parasitol*. (1995) 25 1363-1367

14 Echevarria F, Borba M F S, Piñheiro A C, Waller P J, Hansen J W, The prevalence of anthelmintic resistance in nematode parasites in sheep in southern Latin America: Brazil. *Vet. Parasitol.*, (1996). 62, 199-206.

15 Echevarria F, Unpublished observations (1996)

16 Eddi C, Caracostantologo J, Peña M, Shapiro J, Marangunich L, Waller P J, Hansen J W, The prevalence of anthelmintic resistance in nematodes parasites in sheep in southern Latin America: Argentina. *Vet. Parasitol.* (1996)., 62, 189-197.

17 Eddi C, Unpublished observations (1996)

18 Nari A, Franchi M, Rizzo E, Marmol E, Mautone G, Evaluación de un programa de control de nematodes gastrointestinales en ovinos. Medidas para dilatar la aparición de resistencia antihelmintica. XXV Congreso Nacional de Buiatria. 18-21 de junio 1997, Paysandú. (1997). Uruguay. 98-101.

19 Barger I A, The role of epidemiological knowledge and grazing management for helminth control in small ruminants, *Int. J. Parasitol.* (1999) 29 41-47

20 Melander A L, Can insects become resistant to sprays? *J. Econ. Entomol.* (1914) 7, 167-173.

21 Georghiou G P & Lagunes-Tejeda A, The ocurrence of resistance to pesticides in arthropods. FAO/Univ. Calif. USA. (UN 17/26 IL 2/2 AGPP) (1991). 318.

22 Sangster N C, Anthelmintic resistance: past, present and future. *In*: Novel approaches to the control of helminth parasites of livestock. Proceedings of the Second International Conference. Lousiana University. Baton Rouge. 22-26 March 1998. 28.

23 Waller P J, Sustainable helminth control of ruminants in developing countries. *Vet. Parasitol.*, (1997) 71, 195-207.

24 Barger I A, Control by management. *Vet. Parasitol.* (1998) 72, 493-500.

25 Waruiru R, Kogi J K, Weda E H, Ngotho J W, Multiple anthelmintic resistance on a goat farm in Kenya, *Vet. Parasitol.* (1998) 75, 191-197.

26 Cheneau Y, The effect of structural adjustment programmes on the delivery of Veterinary Services in Africa. 13th Conference of the OIE Regional Commission for Africa, Dakar, 26-29 January 1999. (1999) 7.

27 Fleming E & Patrick I, Rationale and means of goverment intervention in small ruminant development through health improvements. *In*: L.F. Le Jambre & M.R. Knox (Eds). Sustainable parasite control in small ruminants Bogor. Indonesia. (1996) 39-48

28 De Alva R, Creating new products for animal health. *In*: S. Rodriguez Camarillo & H. Fragoso Sanchez (Eds). III Seminario Internacional de Parasitologia Animal. Acapulco. Mexico. 11-13 octubre de 1995. (1995). 86-87.

29 Soll M D, The future of anthelmintic therapy from an industry perspective. *In*: van Wyk J.A & van Schalkwy (Eds.). Managing anthelmintic resistance in endoparasites. 16th International Conference of the World Association for the Advancement of Veterinary Parasitology (1997). 1- 4.

30 Floate K D, Off-target effects of ivermectin on insects and on dung degradation in southern Alberta, Canada. *Bull. Ent. Reas.*, (1998) 88, 25-35.

31 Sprat D M, Endoparasites control strategies: implications for biodiversity of native fauna. *Inter. J. Parasitol.*, (1997). 27, 173-180.

32 Kunz S E & Kemp D H, Insecticides and acaricides: resistance and environmental impact. *Rev. sci. tech. Off. int. epiz.*, (1994). 13, 124-128.

33 Nolan J, Report of the Workshop on Acaricide resistance in the catlle- tick *Boophilus microplus*. FAO/IPVDF. Porto Alegre. Brazil, 21-25 November 1994. (1995). 1-23.

34 Thullner F, Impact of pesticide resistance management based on a regional structure. *World Anim. Rev.*, (1997). 89, 41-47.

35 Nari A, Strategies for the control of one-host ticks and relationship with tick-borne diseases in South America.*Vet. Parasitol.*, (1995) 57 153-165.

36 Sanyal P K, Integrated parasite management in ruminants in India: a concept note. *In*: Hansen J.W. (Ed). Proceeding of a workshop organized by FAO and the Danish Centre for Experimental Parasitology. Ipoh, Malaysia 5-12 October 1997. (1998) 54-65.

37 Dorny P, Claerebout E, Vercruysse J, Sani R, Jalila A, Anthelmintic resistance in goats in peninsular Malaysia. *Vet. Parasitol.*, (1994) 55, 327-342.

38 Himonas C & Papadopoulos E, Anthelmintic resistance in imported sheep. *Vet. Rec.*, (1994) 133 134-156.

39 Requejo-Fernandez J A, Martinez A, Meana A, Rojo-Vazquez F A, Osoro K, Ortega-Mora L M, Anthelmintic resistance in nematode parasites from goats in spain. *Vet. Parasitol.*, (1997). 73, (1/2) 83-88.

40 Yarandy M, Praslicka J, Corba J, Vesely L, Multiple anthelmintic resistance of nematodes in imported goats. *Vet. Rec.*, (1993). 132, 387- 388.

41 Waller P J, International approaches to the concept of integrated control of nematodes parasites of livestock. *Int. J. Parasit.*, (1999). 29, 155-164.

42 Barger I A, Barnes E H, Dobson R J, Modelling anthelmintic resistance. *In*: B.D. Perry & W.J. Hansen. (ed.). Modelling vector-borne and other parasitic diseases. Nairobi: ILRAD. (1990) 177-190.

43 De Castro J J, Sustainable tick and tickborne disease control in livestock improvement in developing countries. *Vet. Parasitol.*, (1997) 71, 77-97.

44 Holmes P H, New approaches to the integrated control of trypanosomosis. *Vet. Parasitol.*, (1997) 71 121-135.

45 Vergara Ruiz R, Sistema de manejo integrado de moscas comunes en explotaciones pecuarias: alternativa ecológica y económica. *En*: Epidemiología, diagnóstico y control de enfermedades parasitarias en bovinos. Compendio II. CORPOICA. Medellín. Colombia. (1996) 41-50.

46 Van Wyk J A, Malan F S, Bath G F, Rampant anthelmintic resistance in sheep in South Africa. What are the options? *In*: van Wyk J.A & van Schalkwy (Eds.). Managing anthelmintic resistance in endoparasites. 16th International Conference of the World Association for the Advancement of Veterinary Parasitology (1997) 51-63.

47 Van Wyk J.A., Krecek R C, Bath G F, Hansen J W, Sustainable worm control programmes, Report of FAO TCP/SAF/8821 Workshop, Pretoria, South Africa, 12-14 June 2000, (2000) 113

48 Kariuki D P, Kiara H K, Muraguri E K, Mwangi E K, Designing control strategies for livestock ticks in Kenya using computer models. International Tick Modelling Workhop. Nairobi. Kenya. 9-19 September 1997. (1997).

49 FAO Expert Consultation on Helminth infections of Livestock in developing Countries. (Report). Rome. Italy, 23-27. September. 1991. (1991) 32.

50 Coles C, Bauer C, Borgsteede F H M, Geerts S, Klei T R, Taylor M A , Waller P J, World Association for the Advancement of Veterinary Parasitology. (W.A.A.V.P) Methods for the detection of anthelmintic resistance in nematodes of veterinary importance. *Vet. Parasitol.*, (1992). 44, 35-44.

51 Kemp D H, Thullner F, Gale K R, Nari A., Sabatini G A, Acaricide resistance in the cattle-ticks *Boophilus microplus* and *Boophilus decoloratus*. Report to the Animal Health Services.FAO. (1998) 1-32.